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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/091,342	03/06/2002	Kevin Burke	7601/80250	1549

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EXAMINER

PROUTY, REBECCA E

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/091,342

Applicant(s)

BURKE ET AL.

Examiner

Rebecca E. Prouty

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 7/03.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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Applicant's election without traverse of Group I, Claims 1-6 in the response filed 5/20/04 is acknowledged.

Claims 7-16 have been canceled. Claims 1-6 are at issue and are present for examination.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 6 are indefinite in the recitation of "intracellular activity of pyruvate oxidase encoded by the poxB gene is decreased or switched off" as "switched off" is non-standard jargon. Is this synonymous with eliminated? This is assumed for purposes of further examination.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to methods of preparing a genus of amino acids (Claim 6) or lysine (claims 1-5) by

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overexpressing a genus of zwf genes in a genus of coryneform bacteria in which the activity of the pyruvate oxidase encoded by the endogenous poxB gene has been reduced or eliminated by a genus of methods.

The specification does not contain any disclosure of the structure and function of all the zwf genes which are overexpressed, nor a disclosure of the structure and methods of preparing of any coryneform bacteria in which the activity of the pyruvate oxidase encoded by the endogenous poxB gene has been reduced or eliminated. The genus of zwf genes encompassed in the instant claims is a large variable genus with the potentiality of encoding many different proteins. Therefore, many structurally and functionally unrelated nucleic acids are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus of zwf genes which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Similarly, genus of coryneform bacteria in which the activity of the pyruvate oxidase encoded by the endogenous poxB gene has been reduced or eliminated is a large variable genus encompassing many different structural modifications of a variety of bacteria. The specification

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discloses only a single species of the claimed genus (i.e., *Corynebacterium glutamicum* DSM5715:pCr.1poxBint/pEC-T18mob2zwf) which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of making lysine using *Corynebacterium glutamicum* containing an inactivating deletion in the endogenous poxB gene and transformed with a nucleic acid encoding the zwf protein of SEQ ID NO:10, does not reasonably provide enablement for methods of making any amino acid using any coryneform bacteria in which the activity of the pyruvate oxidase encoded by the endogenous poxB gene has been reduced or eliminated and any zwf gene is overexpressed. The specification does not enable any person skilled in the art to which it pertains, or with which it is

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most nearly connected, to make the invention commensurate in scope with these claims.

The claims are directed to methods of preparing any amino acid (Claim 6) or lysine (claims 1-5) by overexpressing any *zwf* genes in any coryneform bacteria in which the activity of the pyruvate oxidase encoded by the endogenous *poxB* gene has been reduced or eliminated by any method.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims.

The scope of the claims, as described above, is not commensurate with the enablement provided in regard to the large number of unknown genes and gene modifications required to practice the claimed method. The specification and/or the prior art discloses the structure of the *Corynebacterium glutamicum* *zwf* and *poxB* genes but there is no disclosure in the specification of similar genes isolated from other

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microorganisms, nor there is disclosure of the critical structural elements required in a polynucleotide to encode the proteins corresponding to the genes recited above.

Furthermore, the specification fails to disclose (1) the production of other L-amino acids with the exception of L-lysine, (2) the use of other coryneform microorganisms with the exception of *Corynebacterium glutamicum*, (3) the structure or identity of zwf genes isolated from other organisms and the structure of the endogenous poxB gene of all coryneform microorganisms, (4) how to amplify the intracellular activity of the zwf gene product other than by increasing the copy number of the gene or using a strong promoter, and (5) how to modify the endogenous poxB gene from any coryneform microorganism such that its expression is partially switched off.

Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its

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function. Since structure determines function, one would require some knowledge or guidance as to which are the structural elements required in a polynucleotide to encode a protein of the desired function as well as which are the modifications required in a polynucleotide such that the corresponding protein displays amplified activity or reduced activity, as required by the claims. Also, no disclosure has been provided of which are the modifications in the regulatory elements of the recited genes that would result in reduced expression or increased expression of the desired genes, as recited in the claims. Therefore, due to the lack of relevant examples, the amount of information provided, the lack of knowledge about the critical structural elements and/or structural modifications required to obtain the desired function, and the unpredictability of the prior art in regard to function based on homology, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to (1) isolate the genes, (2) determine the gene modifications required such that their corresponding gene products have increased activity or reduced activity, (3) determine which L-amino acids can be made using the large number of genes and gene modifications encompassed by the claims.

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Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (571) 272-0937. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

A handwritten signature in cursive script, appearing to read 'Rebecca Prouty', with a long horizontal flourish extending to the right.

Rebecca Prouty
Primary Examiner
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